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Contribution to the viral etiology of milker's cowpox.

by T. Nasemann and B. Deubner.

Translated from Hautarzt 4: 210-212 (1953) by the Technical Library Branch, Technical Information Division.

No one doubts today that genuine milker's cowpox is a virus disease. Four different types of virus have been considered as pathogens to date. Some writers assume that the disease is caused by cowpox virus (Frieboes 5, Oppenheim and Fessler 17, Richter and Kressmann 22), others identify the specific causative agent with paravaccinia virus (Katzenellenbogen 10-11, Dolgow and Morosow 6), with variolovaccinia virus or with an attenuated variant of the latter (Cottron 7, Zurukzoglu and Kuske 28, v. Zumbusch 27, Schultze and Grundherr 23, Schultze, Seifried and Schaaf 24), while Petracek (20) suggests a virus sui generis as in the case of infecticus granulomas and warts. Obermayer (cited in Katzenellenbogen 11) even believes that several types of virus (paravaccinia, cowpox, variolovaccinia) may evoke the clinical picture of milker's cowpox. As is well known, milker's cowpox never develops in the course of immunization with variolovaccinia virus, either in man or in animal tests. The vaccinia virus therefore has little significance in the etiology of genuine milker's cowpox. The use of customary lymph vaccines may, under special conditions, lead to occasional abnormal vaccinal reactions characterized by the development of a cherry-red papule. This manifestation is called vaccine rouge in the literature and is attributed to paravaccinia virus. This phenomenon was first pointed out in 1892 by Danve and Larue. More detailed studies date back to 1915 and v. Pirquet. Doubtless there is a closer morphological and clinical relationship between vaccine rouge and milker's cowpox than between the latter and vaccinal efflorescences produced by cowpox virus. It is known that paravaccinia virus cannot be transmitted to test animals and does not reproduce on the chorioallantoic membrane of incubated hen's eggs. Cowpox virus, on the other hand, may be grown on the allantois and gives positive transmission tests (e.g., Paul's corneal test). Paravaccinia virus and cowpox virus therefore are differentiable.

We studied a case of milker's cowpox under our observation with the aim of contributing to the question of the viral etiology of this disease.

All smear preparations revealed numerous elementary bodies (EB), which could not be differentiated from those of animal pox or variolovaccinia (Fig. 2). Due to the relatively late term of investigation, the preparation presumably shows the regenerative phase, in which maximal numbers of EB are no longer present in the tissue. For this reason we saw only isolated EB per field under the electron microscope; these were quite typical, brick-shaped EB between 250 and 280 millimicrons long (Fig. 3). The pathogen of milker's cowpox thus belongs to the class of brick viruses (Tesserulata), and the assumption of a virus sui generis in the sense of Petracek must be rejected. Guarneri bodies were not found during histological examination

of sections. Inoculated rabbits did not produce lesions resembling specific keratitis. In both cases the eyes remained totally unaffected. Cutaneous instillation performed by one of us on himself gave a negative result. Nor was it possible to grow the virus on egg membrane. Not a single allantoic membrane charged with our material showed EB.

These investigations indicate that the observed EB were not those of original cowpox virus, since the latter propagate on the chorioallantois and are demonstrable in the corneal test. Our findings are nearly identical with data recently published by Katzenellenbogen (11). We also believe that the pathogens, which we were able to classify unequivocally as brick viruses, are identical with the organisms called paravaccinia virus in the literature. It is known of the latter that they do not reproduce on the allantois (as is the case also with the virus of molluscum contagiosum) and are not transmissible to test animals. Both molluscum virus and paravaccinia virus may be transmitted from person to person, however. Our negative self-inoculation by the cutaneous route must not be given too much weight, since it was done at a relatively late stage. More important than negative corneal instillations are negative culture results in the egg. Germer (6) emphasized in a compilation that the last-mentioned criterion is far more sensitive than Paul's test. The fact that EB were readily demonstrated light- and electron-optically, but nevertheless did not propagate in the egg, speaks strongly against their classification with the variolovaccinia-cowpox group and for their kinship with paravaccinia. Now, has the concept "paravaccinia" been defined adequately? This question may be affirmed only in the sense that the term includes the pathogen of vaccine rouge, without precise information about its origin. It is assumed to be a modified variolovaccinia virus the original derivation of which is also obscure. The latter either originated from a human smallpox infection and became attenuated in virulence by continuous passages through heifers or calves — or it developed by modification from original cowpox virus. The nature of variolovaccinia virus is changed with relative ease. When rabbits are inoculated intracerebrally with variolovaccinia, followed by continuous brain passages, the virus becomes decidedly neurotropic. These modified pathogens are called neurolapines or neurovaccines, which have acquired additional properties besides a changed tropism. When employed to inoculate rabbit skin, they produce hemorrhagic-necrotic lesions in contrast to the predominantly proliferate manifestations caused by variolovaccinia. Presumably all types of pox are derived from a uniform poxvirus (primordial pox). It is quite likely that the pathogens of variola vera, alastrim, milker's cowpox, vaccine rouge, molluscum contagiosum, and variolovaccinia are only biological modifications (mutants?) of the original poxvirus — as may be the case with various types of animal pox (fowlpox, cow and sheep pox, ectromelia, rabbit myxoma, etc.). It may appear risky to include the virus of molluscum contagiosum and the pathogens of rabbit myxoma in this list. However, considering that all of the aforementioned viruses reveal a uniform structural principle (in spite of certain differences in size) manifested by the typical brick shape and consistent reaction to pepsin (3, 13), the allusion to a possible close relationship seems justified. Differences in clinical symptoms, transmissibility and egg culture may be the result of mutative processes. It may suffice

to point out that the pathogen of milker's cowpox belongs to the class of brick viruses (Tesserulata) and that its properties differ distinctly from those of the variolovaccinia-cowpox virus group, as does the causative organism of vaccine rouge, known as the paravaccinia virus.

Summary

The pathogen of milker's cowpox is identified electron-optically as a brick virus (Tesserulatum).

Illustrations

Fig. 1. Milker's cowpox.

Fig. 2. Light-optical exposure of a smear preparation from efflorescence pictured in Fig. 1, stained according to Fontana-Tribondeau-Morosow. Numerous elementary bodies (magnified 1200 x, oil immersion).

Fig. 3. Electron-optical exposure of isolated elementary bodies. Direct spot preparation with tissue fragments from milker's cowpox (magnified 10000 x).